DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2006 Budget Request

Witness appearing before the
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Mr. Chairman and Members of the Committee, I am pleased to present the Fiscal Year 2006 President's budget request for the NIH AIDS research programs, a sum of $2,932,992,000, which is an increase of $12,441,000 above the comparable FY 2005 appropriation.

WORLDWIDE PANDEMIC

AIDS is the deadliest pandemic of modern times. More than 20 million people have already died of AIDS, and more than 60 million people around the world have been infected with HIV. AIDS is the leading infectious cause of death worldwide, surpassing tuberculosis and malaria.[1] Its impact is profound, affecting families, communities, agriculture, business, healthcare, education, military preparedness, and economic growth. The United Nations General Assembly's Declaration of Commitment on HIV/AIDS states ..."the global HIV/AIDS epidemic, through its devastating scale and impact, constitutes a global emergency and one of the most formidable challenges to human life and dignity, as well as to the effective enjoyment of human rights, which undermines social and economic development throughout the world and affects all levels of society - national, community, family, and individual."[2] According to a UN report, "The misery and devastation already caused by HIV/AIDS is enormous, but it is likely that the future impact will be even greater...The HIV/AIDS epidemic has erased decades of progress in combating mortality and has seriously compromised the living conditions of current and future generations".[3] A CIA report estimated that by 2010, five countries of strategic importance to the U.S. -- Nigeria, Ethiopia, Russia, India, and China -- collectively will have the largest number of HIV/AIDS cases on earth.[4] *Foreign Affairs* magazine stated: "…HIV/AIDS is set to be a factor in the very balance of power within Eurasia -- and thus in the relationship between Eurasian states and the rest of the world".[5] Dramatic increases in HIV infection also are occurring in Eastern Europe, Central Asia, Latin America, and the Caribbean.

THE U.S. EPIDEMIC

In the U.S., according to CDC, the decline in death rates observed in the late 1990s, due largely to expanded use of new antiretroviral therapies (ART), has now leveled off. The use of ART has now been associated with a serious side effects and long-term complications that may have a negative impact on mortality rates. HIV infection rates are continuing to climb among women, racial and ethnic minorities, young homosexual men, individuals with addictive disorders, and people over 50 years of age.[6] This means that the overall epidemic is continuing to expand.[7 8 9] CDC reports that approximately one quarter of the HIV-infected population in the United States also is infected with hepatitis C virus (HCV). HIV/HCV co-infection is found in 50 to 90 percent of injecting drug users (IDUs). HCV progresses more rapidly to liver damage in HIV-infected persons and may also impact the course and management of HIV infection, as HIV may change the natural history and treatment of HCV.[10]

For the past several years, we have cautioned in our testimony that the appearance of multi-drug resistant strains of HIV presents an additional serious public health concern.[11 12 13 14 15] In just the past few weeks, we have had a new warning about that potential. The New York City Health Department reported the possibility of a more virulent and aggressive multi-drug resistant HIV strain[16] focusing attention again upon the nature of the infection, the associated immune decline, and the behaviors linked to HIV transmission. It is too early to determine if this is some newly virulent form of HIV. A series of highly sophisticated tests is now underway to examine how the virus replicates in cells, as well as the efficiency and mechanisms of viral attack. The fact that the individual infected by this virus progressed more rapidly to immune decline may be reflective of a number of factors, some unrelated to the viral strain, such as host factors, native immune system function, or genetics. We have much more to learn about this case. However, it highlights a number of lessons about the active and ongoing U.S. HIV epidemic. HIV infection does not occur in a vacuum or in isolation – it occurs in the context of behaviors, including alcohol and drug use (the use of crystal methamphetamine in the New York City case), that require a contextually

appropriate and interwoven response. This case underscores the importance of access to quality care that may need to include HIV resistance testing, and closer monitoring for immune decompensation in the setting of appropriate treatment. Most importantly, this case is a wake-up call, a reminder that the ability to interrupt HIV transmission, as well as the cycle of pain and suffering associated with HIV disease, is directly related to the robustness of HIV care, treatment and research infrastructure in the communities impacted by this disease. This expanding and evolving U.S. epidemic continues to present new and complex scientific challenges.

ROADMAP FOR NIH AIDS RESEARCH

In response to this worldwide crisis, NIH is the world's leader in the magnitude and quality of our AIDS research effort – a comprehensive program of basic, clinical, and behavioral research on HIV infection, its associated co-infections, opportunistic infections, malignancies, and other complications. No other disease so thoroughly transcends every area of clinical medicine and scientific investigation, crossing the boundaries of nearly all of the NIH Institutes and Centers. The Office of AIDS Research (OAR) plays a unique role at the NIH, establishing a roadmap for the AIDS research program. OAR coordinates the scientific, budgetary, and policy elements of the NIH AIDS program, prepares an annual comprehensive trans-NIH strategic plan and budget for all NIH-sponsored AIDS research; facilitates NIH involvement in international AIDS research activities; and identifies and facilitates multi-institute participation in priority areas of research. These legislative authorities are critical to identify and ensure support for the areas of highest scientific priority.

COMPREHENSIVE AIDS RESEARCH PLAN AND BUDGET

The OAR planning process is inclusive and collaborative, involving the NIH Institutes, eminent non-government experts from academia, industry, foundations, and AIDS community representatives. The Plan serves as the framework for developing the annual AIDS research budget for each Institute and Center, for determining the use of AIDS-designated dollars, and for tracking and monitoring those expenditures. The planning process also serves to monitor and assess scientific progress. The Plan

establishes the NIH AIDS scientific agenda in the areas of: Natural History and Epidemiology; Etiology and Pathogenesis; Therapeutics; Vaccines; and Behavioral and Social Science; Microbicides; Racial and Ethnic Minorities; Women and Girls; Prevention Science; International Research; Training, Infrastructure, and Capacity Building; and Information Dissemination.

In consultation with the Director of NIH, the OAR determines the total annual AIDS research budget. The Institutes and Centers submit their AIDS budget request to OAR, and the OAR establishes their AIDS research budgets, in accordance with the priorities of the Plan, at each step of the budget development process.

FUNDING FOR HIGHEST PRIORITY RESEARCH

To develop the FY 2006 request, OAR initiated a comprehensive trans-NIH review of all grants and contracts supported with AIDS-designated funds to ensure that these projects represent the highest scientific priorities and opportunities. OAR carefully reviewed the mix of investments in key priority areas of research in view of the current epidemic. This budget request reflects OAR's redirecting of AIDS funds to the highest priority projects and new scientific opportunities in FY 2006.

This budget request places highest priority on the discovery, development, and testing of additional HIV vaccine candidates, including funding to move promising vaccine candidates into large-scale clinical trials to evaluate the potential for efficacy. The NIH priority in AIDS vaccine research to date has resulted in approximately 70 clinical trials of nearly 40 vaccine candidates. The evaluation of an AIDS vaccine will require extensive testing in the United States and in international settings where there is a high incidence of HIV.

In the area of therapeutics research, current drug regimens have resulted in extended survival and improved quality of life for many HIV-infected individuals in the U.S. and Western Europe. However, a growing proportion of patients receiving therapy are demonstrating treatment failure, experiencing serious drug toxicities and side effects, and developing drug resistance. The increasing incidence of metabolic

disorders, cardiovascular complications, major organ dysfunction, and physical changes associated with current antiretroviral drugs underscores the critical need for new and better treatment regimens. Improved regimens also are needed to treat HIV co-infections such as hepatitis B and C, as well as other opportunistic infections to reduce drug interactions and problems with adherence to complicated treatment regimens. The goal of this research is to develop new, safe, less toxic, less expensive, and more effective therapeutic agents and regimens.

OAR spearheaded a multi-IC inter-disciplinary collaboration to formalize plans for the restructuring of the NIH clinical trials networks for HIV therapeutics, vaccines and prevention. This effort resulted in a set of principles to guide the development of the Request for Applications (RFAs) for the re-competition of these essential multi-IC supported clinical programs in FY 2006, designed to ensure that they operate effectively and cooperatively, making the best use of research dollars.

Our prevention research priorities include the development of vaccines, topical microbicides, strategies to prevent mother-to-child transmission, including a better understanding of risk associated with breast-feeding, management of sexually transmitted diseases (STDs), and behavioral research strategies, including interventions related to drug and alcohol use. Efforts continue to identify the most appropriate intervention strategies for different populations and sub-epidemics in the U.S. and around the world.

INTERNATIONAL AIDS RESEARCH

NIH bears a unique responsibility to address the global epidemic, with priority on the urgent need for more affordable and sustainable prevention and treatment approaches that can be implemented in resource-limited nations. The high incidence of Hepatitis B and C, malaria, and TB in many of these nations further complicates the treatment and clinical management of HIV-infected individuals. NIH international AIDS research includes: development of HIV vaccine candidates and chemical and physical barrier methods, such as microbicides; behavioral strategies; strategies to prevent mother-to-child transmission; therapeutics for HIV-related co-infections and

other conditions; and approaches to using ART in resource-poor settings. NIH supports international training programs and initiatives that help build research infrastructure and laboratory capacity.

WOMEN AND MINORITIES

In the U.S., the rate of diagnoses for African Americans was almost 10 times the rate for whites and almost 3 times the rate for Hispanics. The rate of AIDS diagnoses for African American women was 25 times the rate for white women.[17] Women experience HIV/AIDS differently than men. NIH research has demonstrated that women progress to AIDS at lower viral load levels and higher CD4 counts than men. Women also experience different clinical manifestations and complications of HIV disease. These findings may have implications for care and treatment of HIV-infected women, particularly with ART. NIH is exploring research questions about specific characteristics of women and girls that might play a role in transmission, acquisition, or resistance to HIV infection during different stages of the life course. We are focusing on the need for comprehensive strategies to decrease HIV transmission in affected vulnerable populations, and improve treatment options and treatment outcomes, including interventions that address the co-occurrence of other STDs, hepatitis, drug abuse, and mental illness; and interventions that consider the role of culture, family, and other social factors in the transmission and prevention of these disorders in minority communities. NIH continues to make significant investments to improve research infrastructure and training opportunities for minorities and will continue to ensure the participation of minorities in AIDS clinical trials, as well as in natural history, epidemiologic, and prevention studies.

SUMMARY

The NIH's leadership role in the response to the AIDS pandemic is fundamental and unprecedented, and we have established a research program that is complex, comprehensive, multi-disciplinary, inter-disciplinary, and global. Further, this research investment is reaping even greater dividends, as AIDS-related research is also unraveling the mysteries surrounding many other infectious, malignant, neurologic,

autoimmune, and metabolic diseases. The legislative authorities of the OAR allow NIH to pursue a united research front against the global AIDS epidemic. NIH is enhancing collaboration, minimizing duplication, and ensuring that research dollars are invested in the highest priority areas of scientific opportunity that will allow NIH to meet its scientific goals. We are deeply grateful for the continued support the Administration and this Committee have provided to our efforts.

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Dr. Whitescarver received his doctorate in medical microbiology in 1974 from the University of Medicine and Dentistry of New Jersey (UMDNJ), Graduate School of Biomedical Sciences. He pursued his post-doctoral research at the Harvard School of Public Health, focusing on immunopathogenesis of rickettsia infection. In his position as a Research Associate at the Harvard School of Public Health and Medical School, Dr. Whitescarver's research interests included obligate intracellular parasites. His published research results include in vitro studies on breast tumors, spirochetes, mycoplasmas, and rickettsia.

In 1977, Dr. Whitescarver completed a year in the Grants Associates Program at the National Institutes of Health (NIH) and became the Special Assistant to the Director of the National Institute of Allergy and Infectious Diseases (NIAID). In that position he was responsible for assisting the Director in policy, planning and budget issues. It was during this tenure that Dr. Whitescarver first reported to the NIAID on the possibility of the emergence of a new infectious disease, now known as AIDS, and he helped develop the initial federal response for research on AIDS.

From 1984 to 1988, Dr. Whitescarver held the positions of Associate Dean for Research Development and Assistant Professor of Pathology at Emory University School of Medicine. His duties as Associate Dean included directing the M.D. /Ph.D. training program and facilitating new research initiatives, particularly in AIDS.

In 1988, the new Office of AIDS Research (OAR) at the NIH was established, and Dr. Whitescarver was recruited as the Deputy Director. He served as Acting Director of the OAR from October 2000 until June 2002, when he was named permanent Director. In response to the AIDS pandemic, NIH has developed a comprehensive biomedical and behavioral research program to better understand the basic biology of HIV, develop effective therapies to treat it, and design interventions to prevent new infections from

occurring. It is the role of the OAR to plan and coordinate this research program sponsored by all of the more than twenty NIH Institutes and Centers.
Dr. Whitescarver is a member of several professional societies including the American Academy of Allergy and Immunology, Infectious Diseases Society of America, and the International AIDS Society. He has received numerous honors and awards including the Alumnus of the Year Award from the UMDNJ Graduate School of Biomedical Sciences and the Award for Distinguished Service from the Secretary of the Department of Health and Human Services.

Department of Health and Human Services
Office of Budget

William R. Beldon

Mr. Beldon is currently serving as Deputy Assistant Secretary, Budget in the Department of Health and Human Services. He has been a Division Director in the Budget Office for sixteen years, most recently as Director of the Division of Discretionary Programs. Mr. Beldon started in federal service as an auditor in the Health, Education and Welfare Financial Management Intern program. Over the course of more than 30 years in the Budget Office, Mr. Beldon has held Program Analyst, Branch Chief and Division Director positions. Mr. Beldon received a Bachelor's Degree in History and Political Science from Marshall University and attended the University of Pittsburgh where he studied Public Administration. He resides in Fort Washington, Maryland.Mr. Beldon is currently serving as Deputy Assistant Secretary, Budget in the Department of Health and Human Services. He has been a Division Director in the Budget Office for sixteen years, most recently as Director of the Division of Discretionary Programs. Mr. Beldon started in federal service as an auditor in the Health, Education and Welfare Financial Management Intern program. Over the course of more than 30 years in the Budget Office, Mr. Beldon has held Program Analyst, Branch Chief and Division Director positions. Mr. Beldon received a Bachelor's Degree in History and Political Science from Marshall University and attended the University of Pittsburgh where he studied Public Administration. He resides in Fort Washington, Maryland.